January 21, 2005

Recommendations for presumptive treatment of schistosomiasis and strongyloidiasis among the Lost Boys and Girls of Sudan

Summary

Based on the findings of a recent investigation in which a high prevalence of schistosomiasis and strongyloidiasis was found among the Lost Boys and Girls of Sudan refugee group, to prevent future morbidity from these diseases, CDC recommends that members of the Lost Boys and Girls of Sudan refugee group who have resettled to the U.S. receive presumptive treatment for schistosomiasis and strongyloidiasis. Treatment for schistosomiasis should consist of praziquantel (Biltricide®) at a dose of 20 mg/kg, given in two oral doses 6-8 hours apart. Treatment of strongyloidiasis should consist of albendazole (Albenza®) at a dose of 400 mg, given in oral doses, twice a day for 3 days. This document provides background information on the investigation, rationale for the recommendations, and technical information for physicians.

Introduction

During the civil war in Sudan, which began approximately 25 years ago, thousands of people became either internally displaced or refugees. Beginning in the mid-1980's, one group of displaced Sudanese, which was mostly composed of children and young adults, became known as the Lost Boys and Girls of Sudan. During a journey of several years, the Lost Boys and Girls walked first to Ethiopia and later to Kenya or to Egypt. Many arrived at the Kakuma refugee camp in western Kenya in 1992. From Kakuma, the United States resettled approximately 3,800 Lost Boys and Girls from 2000 through 2001. Lost Boys and Girls have also entered the U.S. through other refugee resettlement channels and from different locations. Approximately 3,800-5,000 Lost Boys and Girls are currently living in the U.S. Not all Sudanese refugees are Lost Boys or Girls. However, it may be difficult to distinguish between Lost Boys and Girls and other Sudanese refugees. CDC recommends that Lost Boys and Girls and Sudanese refugees from similar circumstances receive presumptive therapy for schistosomiasis and strongyloidiasis. CDC is currently in the process of developing more formal guidance pertaining to other refugees from Africa.

In 2004, the Division of Global Migration and Quarantine (DGMQ), Centers for Disease Control and Prevention (CDC) received reports from multiple sources that many of these Lost Boys and Girls refugees were complaining of chronic abdominal pain. However, the prevalence and characteristics of this pain among these refugees had not been systematically evaluated. Informal discussions with public health officials, state refugee health coordinators, and physicians have suggested the etiology is multifactorial. Infectious diseases, variations in post-arrival health assessments and access to healthcare, and important psychosocial issues may all be contributing to the problem. Schistosomiasis and strongyloidiasis are parasitic diseases that are endemic in most of

the world's tropical areas, including Sudan. In July 2004, CDC received reports of two Lost Boys with chronic abdominal pain who were diagnosed with *Schistosoma mansoni* following gastrointestinal tract biopsies, raising the possibility of schistosomiasis as one potential cause of chronic abdominal pain among these refugees. Because of its relatively high prevalence among refugee populations, strongyloides infection was also considered as another potential cause of this pain.

Information about the incidence and prevalence of schistosomiasis and strongyloidiasis among the Lost Boys and Girls of Sudan is limited. Refugees from Africa are typically not tested pre-departure for intestinal parasitic infections; instead, before departure from their host country for resettlement in the United States, they receive presumptive treatment for intestinal parasites. This policy is based upon previous prevalence surveys among African refugees and cost-effectiveness analyses, which demonstrated that presumptive pre-departure treatment of all at-risk refugees was the most cost-effective approach for managing intestinal parasitic infections among migrants.[1,2,3] The current pre-departure presumptive treatment regimen for intestinal parasites consists of a single dose of albendazole; however, this regimen does not adequately treat either schistosomiasis or strongyloidiasis. Refugees also receive a domestic health assessment, usually conducted at state or local health departments, within three months of U.S. arrival. At present, there is no standardized nationwide protocol for the post-arrival health assessment, and the content of this assessment varies from state to state and at the local clinic level. In an informal survey of post-arrival screening procedures, several states reported performing testing for schistosomiasis or strongyloidiasis through stool examination. Most refugees receive a stool examination for parasite infections; however, due to sensitivity problems, stool examination may not identify the parasites for schistosomiasis or strongyloidiasis. One clinic reported routine serologic testing for these infections and diagnosed schistosomiasis in approximately 10% and strongyloidiasis in approximately 8% of a subset of age-appropriate Sudanese refugees (presumed to be Lost Boys and Girls).

In response to these reports, the Arizona Department of Health Services and the Office of Global Health Affairs (OGHA), Department of Health and Human Services (DHHS) requested the assistance of the Division of Global Migration and Quarantine (DGMQ) and the Division of Parasitic Diseases (DPD), National Center for Infectious Diseases, to investigate the prevalence of chronic abdominal pain, schistosomiasis, and strongyloidiasis among the Lost Boys and Girls of Sudan. Arizona, which received approximately 400 Lost Boys and Girls during the resettlement, requested assistance with an investigation and intervention during a national reunion of Lost Boys and Girls held August 26-29, 2004, in Phoenix, Arizona.

Epidemiologic Investigation during the Lost Boys and Girls Reunion, Arizona, 2004

Methods

During the Lost Boys and Girls Reunion, the refugees were invited to participate in a survey designed to determine the prevalence of chronic abdominal pain. Reunion attendees were also given the opportunity to have a blood test for schistosomiasis and strongyloidiasis. The tests performed were CDC ELISA serologic tests. The schistosomiasis test is 99% and 90% sensitive in detecting antibodies to *Schistosoma mansoni* and *S. haematobium*, respectively. The test for strongyloidiasis is 95%

sensitive in detecting antibodies to *Strongyloides stercoralis*. While the sensitivity and specificity of stool tests for either schistosomiasis or strongyloidiasis and urine tests for *S. haematobium* can vary depending on the number and technique of the tests performed, these CDC serologic tests have much greater sensitivity. Both these tests are available only at CDC; no locally available serologic tests for schistosomiasis or strongyloidiasis have known reliability. Testing for schistosomiasis was performed by CDC laboratorians using CDC reagents and equipment at the Arizona Department of Health Services Laboratory, while testing for strongyloidiasis was performed entirely at CDC.

Test results for schistosomiasis were available during the reunion, and treatment was offered to those who tested positive. Treatment consisted of praziquantel (20 mg/kg) in two oral doses separated by 6-8 hours. Bayer Pharmaceuticals Corporation donated the praziquantel for this limited pilot evaluation.

Preliminary Results

Four hundred sixty-six Lost Boys and Girls participated in the survey. Among the participants who completed the survey, 214 (46%) reported experiencing chronic abdominal pain since resettlement.

Four hundred sixty-four Lost Boys and Girls participated in the laboratory testing. Antibodies to *S. mansoni* or *S. haematobium* were detected in 204 (44%) of the refugees tested. Two hundred twenty-seven (49%) of the 464 participants tested positive for strongyloidiasis by serology. Overall, 103 (22%) of Lost Boys and Girls were seropositive for both schistosomiasis and strongyloidiasis, and 315 (69%) were seropositive for either parasitic infection.

One hundred eighty (88%) of the refugees who tested positive for schistosomiasis received treatment during the reunion. Those with positive tests who were not treated during the reunion are receiving treatment through collaboration with the appropriate state and local health departments. The refugees will receive notification of their strongyloidiasis results from late November through early December, and will also receive treatment for strongyloidiasis through collaboration with the appropriate state and local health departments.

Data from the survey are currently being analyzed to determine what associations with chronic abdominal pain exist. In addition, a post-treatment follow-up survey is planned.

The high proportion of chronic abdominal pain in this population, however, cannot be attributed to the presence of these infections. The proportion of these infections is nearly the same among participants with chronic abdominal pain and those without chronic abdominal pain. The prevalence ratio of chronic abdominal pain for participants with schistosomiasis is 0.97 (95% CI: 0.80-1.19)**;** for strongyloidiasis, 0.98 (95% CI: 0.80-1.19); for participants co-infected, 0.93 (95% CI: 0.73-1.19); for participants with either infection, 1.00 (95% CI: 0.81-1.24). Thus, while schistosomiasis and strongyloidiasis are highly prevalent among Lost Boys and Girls, physicians cannot assume that these infections are the sole cause of their patient's chronic abdominal pain.

Recommendations for Presumptive Treatment of Schistosomiasis and Strongyloidiasis among the Lost Boys and Girls of Sudan

Due to the high prevalence of schistosomiasis and strongyloidiasis found among the Lost Boys and Girls of Sudan, and to prevent future morbidity from these diseases, CDC recommends that members of the Lost Boys and Girls of Sudan refugee group who have resettled to the U.S. and were not tested at the reunion receive presumptive treatment for schistosomiasis and strongyloidiasis. Treatment for schistosomiasis should consist of praziquantel at a dose of 20 mg/kg, given in two oral doses 6-8 hours apart. Treatment of strongyloidiasis should consist of albendazole at a dose of 400 mg, given in oral doses, twice a day for 3 days. Patients of all ages may take these medications. Table 1 provides a summary of the recommendations. To help determine the effectiveness of this intervention, physicians are requested to report to DGMQ the state of residence, age, and gender of Lost Boys and Girls who receive presumptive therapy.

Although data analysis is ongoing and the presence of schistosomiasis and strongyloidiasis is not correlated with chronic abdominal pain in this population, the high prevalence of both infections found among the Lost Boys and girls screened nonetheless warrants intervention. Urgent dissemination of preliminary results and recommendations for management of the remainder of the cohort of the Lost Boys and Girls of Sudan to physicians caring for these refugees is the purpose of this document. Without treatment, both schistosomiasis and strongyloidiasis can lead to significant morbidity, such as liver failure from chronic schistosomiasis infection and the hyperinfection syndrome in immunocompromised persons with strongyloides infection, and it is therefore important to treat persons with these parasitic infections, even when asymptomatic.

Several options for managing these parasitic infections among the Lost Boys and Girls of Sudan are currently available and were considered for implementation: selective screening and treatment; universal screening for all refugees, with treatment of those who screen positive; and presumptive treatment of all refugees. The high prevalence of these infections among the Lost Boys and Girls of Sudan and the lack of correlation between infection and symptoms such as chronic abdominal pain make the option of selective screening unfeasible in this situation. The second option of universal screening of the Lost Boys cohort and treatment of those who test positive was also considered, but would be impossible to implement because reliable serologic tests are not locally available and the CDC laboratory does not have the reagents or capacity to perform testing on this scale. The third option of presumptive treatment of all refugees is the most viable option, based both on the high prevalence of infections found among the Lost Boys and Girls and the safe and successful use of presumptive therapy among numerous populations in the past decade.

The use of presumptive therapy is a standard public health tool that has been applied safely and effectively both in the United States and globally, including among refugee populations. For example, in the United States, presumptive therapy is provided to partners of persons with selected sexually transmitted infections. Globally, the World Health Organization (WHO) conducts mass therapy campaigns with praziquantel as part of its worldwide schistosomiasis control effort.[4] Albendazole has also been administered presumptively to hundreds of thousands of persons in areas of endemic disease and has not been reported to cause side effects requiring medical attention in field trials.[3,5]

Finally, CDC currently recommends pre-departure presumptive treatment for malaria and intestinal parasites for refugees coming from Africa and Southeast Asia, and evaluations of this pre-departure presumptive treatment program have documented significant decreases in intestinal helminths.[6]

While ivermectin (Stromectol®) is considered the drug of choice for treatment of strongyloidiasis, CDC is not recommending this drug for presumptive treatment for strongyloidiasis in the Lost Boys and Girls because of concerns about potential concurrent *Loa loa* infection (a filarial parasite transmitted by the tabanid fly in Western and Central Africa). Persons who have high levels of microfilaremia associated with *Loa loa* infection may have a life-threatening encephalopathic reaction if treated with ivermectin. Thus, ivermectin should not be given to a Lost Boy or Girl unless *Loa loa* microfilaremia has been ruled out. The preferable method of diagnosis of *Loa loa* infection is a daytime blood smear for circulating microfilariae performed by an experienced laboratorian. Because the prevalence of *Loa loa* infection among the Lost Boys and Girls is unknown and testing for *Loa loa* is not widely available, CDC recommends albendazole, which does not cause adverse reactions in persons infected with *Loa loa,* for the presumptive treatment of strongyloidiasis in this population.

Follow-up testing for schistosomiasis or strongyloidiasis is not routinely necessary in this population after presumptive treatment for these diseases is completed. However, persons who have symptoms that suggest failure of cure or morbidity from these diseases should have appropriate follow-up testing performed. Such patients should be under the care of a physician; CDC physicians are available to provide guidance to physicians in these situations.

In addition, persons who are immunocompromised or may become immunocompromised in the near future, including persons with AIDS, HIV infection, cancer, chronic steroid users, and persons who have had a transplant or who may receive a transplant are at high risk for *Strongyloides* hyperinfection syndrome. All Lost Boys and Girls should be counseled about this risk, and refugees who are immunocompromised should seek follow-up care with their primary physician. Although routine follow-up testing is not necessary for non-immunocompromised Lost Boy and Girl refugees, immunocompromised persons should have a serologic test for *Strongyloides* performed by CDC at least 6 months after treatment to ensure cure has occurred. All Lost Boys and Girls should be counseled that if they become immunocompromised in the future, *Strongyloides* testing should be performed at that time to rule out ongoing strongyloidiasis.

Precautions and Contraindications to Presumptive Treatment

Persons who have cysticercosis infection may have a seizure following treatment with praziquantel or albendazole because these medications can kill *Taenia solium* cysticerci, thus provoking seizure activity. The prevalence of cysticercosis among the Lost Boys and Girls is unknown but is believed to be low based on the known geographic distribution of cysticercosis. Refugees with a history of seizures who have not been evaluated for cysticercosis should be evaluated before receiving these drugs. Refugees with cysticercosis should not receive presumptive treatment and should have serologic testing for schistosomiasis and strongyloidiasis performed at CDC.

Pregnant women should not receive praziquantel or albendazole; they should have serologic testing for schistosomiasis and strongyloidiasis performed at CDC. Praziquantel is a pregnancy category B drug, while albendazole is a pregnancy category C drug. Women of childbearing age who are concerned about being pregnant should have a negative pregnancy test prior to administration of these medications. Women who are breast-feeding should not nurse their infants until 72 hours after treatment withpraziquantel. Because it is unknown whether albendazole is excreted in human milk, caution should be exercised when albendazole is administered to a nursing woman.

Conclusion

CDC recommends that members of the Lost Boys and Girls of Sudan refugee group receive presumptive treatment for schistosomiasis and strongyloidiasis. Treatment for schistosomiasis should consist of praziquantel at a dose of 20 mg/kg, given in two oral doses 6-8 hours apart. Treatment of strongyloidiasis should consist of albendazole at a dose of 400 mg, given in oral doses twice a day for 3 days. Patients with a seizure disorder that has not been evaluated for cysticercosis should be evaluated before receiving these drugs. Lost Boys and Girls who have a history of cysticercosis or are pregnant should not receive presumptive treatment and should have serologic testing for schistosomiasis and strongyloidiasis performed at CDC. Refugees who test positive for these infections should have a treatment plan developed in coordination with a physician. Patients who are immunocompromised should have follow-up serology for *Strongyloides* at least six months after treatment to ensure cure has been successful. If patients become immunocompromised in the future, *Strongyloides* testing should be performed at that time to rule out ongoing strongyloidiasis. CDC can provide additional consultation as needed for these patients or patients for whom presumptive therapy may have failed. Physicians should be aware that treating these infections may not eliminate chronic abdominal pain that a Lost Boy or Girl is experiencing.

To help determine the effectiveness of this intervention, physicians are requested to report to DGMQ the state of residence, age, and gender of Lost Boys and Girls who receive presumptive therapy.

For questions regarding these recommendations and to report treatments provided, please contact Dr. Drew Posey at the Division of Global Migration and Quarantine (404-498-1601; dposey@cdc.gov).

References

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Table1. Recommendations for presumptive treatment of schistosomiasis and strongyloidiasis among the Lost Boys and Girls of Sudan.

	Presumptive Treatment		CDC Testing for Schistosomiasis and Strongyloidiasis		
Group	Schistosomiasis	Strongyloidiasis	Before Therapy	After Therapy	Needs Follow-up After Therapy
Healthy	Praziquantel 20 mg/kg, two oral doses 6-8 hours apart	Albendazole 400 mg, oral doses, twice a day for 3 days	No	If patient becomes immune compromised: test for strongyloidiasis	If patient becomes immune compromised: test for strongyloidiasis
Immune compromised*	Praziquantel 20 mg/kg, two oral doses 6-8 hours apart	Albendazole 400 mg, oral doses, twice a day for 3 days	No	Strongyloidiasis testing at least 6 months after treatment	Testing for strongyloidiasis at least 6 months after treatment
Seizure disorder not evaluated for cysticercosis*	Evaluate for cysticercosis before giving therapy	Evaluate for cysticercosis before giving therapy	No	No	No
Seizure disorder not caused by cysticercosis	Praziquantel 20 mg/kg, two oral doses 6-8 hours apart	Albendazole 400 mg, oral doses, twice a day for 3 days	No	If patient becomes immune compromised: test for strongyloidiasis	If patient becomes immune compromised: test for strongyloidiasis
Cysticercosis*	No	No	Yes	No	No
Pregnant women*	No	No	Yes	No	No

* CDC can provide additional consultation as needed for these patients or for patients for whom presumptive therapy may have failed.

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